UNITED STATES DISTRICT COURT FOR THE DISTRICT OF NEW JERSEY

MUTUAL PHARMACEUTICAL COMPANY, INC., et al.

Plaintiffs.

v.

WATSON PHARMACEUTICALS, INC., et al.
Defendants.

Civil Action No. 09-5421(GEB)(TJB)

DECLARATION OF MICHAEL RAYA IN SUPPORT OF DEFENDANT WEST-WARD PHARMACEUTICAL CORP.'S MOTION FOR SUMMARY JUDGMENT

- I, Michael Raya, declare and state as follows:
- 1. I am the Corporate Vice President and Chief Executive Officer for West-Ward Pharmaceutical Corp. ("West-Ward"), a generic drug company headquartered in Eatontown New Jersey. I have been employed by West-Ward since 1992.
- 2. I am of the age of majority and competent to give the testimony contained herein. The testimony herein is based upon my own personal knowledge.
- 3. West-Ward has manufactured and distributed generic drugs since 1947, holds at least 60 active abbreviated new drug applications (ANDAs) approved by the Food and Drug Administration's (FDA) Office of Generic Drugs, and markets a total of 56 distinct drug products.
- 4. While the vast majority of drugs manufactured by West-Ward are approved by FDA, for historical reasons arising from changes to the Federal Food Drug and Cosmetic Act (FFDCA), and the gradual evolution of FDA's responsibilities and authority, some of West-Ward's drugs were never formally approved. One such unapproved drug is colchicine tablets (0.6 mg), which West-Ward has manufactured since at least 1972.
 - 5. West-Ward is the leading supplier of colchicine tablets in the United States, and has

sold more than a billion colchicine tablets since 1972.

- 6. FDA is well aware that West-Ward manufactures and distributes colchicine tablets in the United States.
- 7. West-Ward's colchicine tablets have been registered on the FDA's National Drug Code Directory, under NDC code 00143-1201, since at least 1979. FDA has inspected the facility where West-Ward manufactures colchicine tablets at least 27 times since 1995, and West-Ward has filed with FDA reports of adverse events for its colchicine tablets.
- 8. West-Ward has never received a Warning Letter or other communication from the FDA questioning West-Ward's failure to secure approval for its colchicine tablets, the legality of West-Ward's colchicine, or West-Ward's right to continue to market its colchicine.
- 9. As a generic drug company, West-Ward does not market its colchicine tablets in the customary sense of that term. Rather, it sells colchicine tablets, as it does with its other generic drugs, based solely on competitive pricing.
- 10. The only "promotional" materials distributed by West-Ward relating to its colchicine tablets are catalogs that contain a list of available drugs and corresponding prices. West-Ward's colchicine tablets also appear on wholesaler ordering systems and various price lists such as First DataBank that report the availability of West-Ward's product.
- 11. Generally, the only information presented in these product listings is the product name, strength, package size, NDC number, price and manufacturer.
- 12. Occasionally, some of the wholesaler ordering systems and price lists will report a therapeutic equivalency rating for a product, as such rating is reported by the FDA in its Orange Book. Wholesaler ordering systems and price lists will sometimes report an "N/A" or "NR" in

By law, every drug manufacturer is required to report the drugs it manufactures to FDA, and FDA assigns a unique NDC code to all submitted drugs. FDA publishes these NDC codes on the internet at http://www.fda.gov/Drugs/InformationOnDrugs/ucm142438.htm

this field. Based on my knowledge and experience in the drug industry, these are short hand for "not applicable" or "not rated," to reflect the fact that FDA has not made a finding of equivalence, or that the drug has not gone through the FDA approval process.

- 13. To my knowledge, none of the catalogs, price lists or wholesaler ordering systems reports or has ever reported West-Ward's colchicine products as FDA approved.
- 14. West-Ward manufactured and sold approximately 35,000,000 colchicine tablets to Mutual Pharmaceutical Company, Inc. and its affiliates ("Mutual") between 1993 and 1998. None of those tablets was approved by the FDA.
- 15. A true and correct copy of the prescribing information (a/k/a package insert) that accompanied the tablets West-Ward manufactured for Mutual in 1998 is attached hereto in Exhibit A.
- 16. A true and correct copy of the prescribing information (a/k/a package insert) that accompanies West-Ward's colchicine tablets, as revised in June 2008, is attached hereto as Exhibit B.
- 17. Based on my review of information reported by Medi-Span after this case was filed, I confirmed that Mutual also marketed unapproved colchicine tablets from February 1999 until July 2006 under NDC 00677-1683 and NDC 00677-1962. A true and correct copy of the information I reviewed is attached hereto as Exhibit C.

I declare under penalty of perjury under the laws of the United States that the foregoing is true and correct.

Executed at Eatontown, New Jersey, on July <u>2/</u>, 2010.

Michael Raya

EXHIBIT A

patient usually remains conscious. However, delirium and convulsions may occur. Death usually is the result of respiratory depression.

Recent studies appear to support the use of hemodialysts or peritoneal dialysis as part of the treatment of acute overdosage. Shock must be combated. Atropine and morphine may relieve the abdominal pain. Respiratory assistance may be needed to insure proper oxygenation and ventilation.

DOSAGE AND ADMINISTRATION: Colchicine should be started at the first warning of an acute attack; a delay of a few hours impairs its effectiveness. The usual adult dose is 1 or tablets initially, followed by 1 tablet every one to two hours until pain is relieved or nausea, vomiting, or diarrhea develops. Some physicians use 2 tablets every two hours. Since the number of doses required may range from six to 16, the total cose is variable. As interval treatment, 1 tablet may be taken one to four times a week for the mild or moderate case, once or twice daily for the severe case.

HOW SUPPLIED: Colchicine Tablets USP 0.6 mg: White, round, unscored compressed tablet imprinted "West-ward 201".

Bottles of 100 tablets. Bottles of 250 tablets. Bottles of 1000 tablets. Unit Dose Boxes of 100 tablets.

Store at controlled room temperature 15°-30°C (59°-86°F). Protect from light and moisture. Dispense in a tight, light-resistant container as defined in the USP using a child-resistant

P_X only

Colchicine is extremely poisonous.

Manufactured by: West-ward Pharmaceutical Corp. Eatontown, NJ 07724 Revised May 1998 COLCHICINE TABLETS, USP Revised 05/98

DESCRIPTION: A phenanthrene derivative, colchicine is the active alkaloidal principie derived from various species of Colchicum; it appears as pale-yellow amorphous scales or powder that darkens on exposure to light.



The molecular formula is $C_{22}H_{25}NO_{8}$ (399.44). One g dissolves in 25 ml of water and in 220 ml of either. Colchicine is freely soluble in alcohol and chloroform.

Colchicine, an acetyltrimethylcolchicinic acid, is hydrolyzed in the presence of dilute acids or alkalies, with cleavage of a methyl group as methanol and formation of colchicelne, which has very little therapeutic activity. Or hydrolysis with strong acids, colchicine is converted to trimethylcolchicinic acid.

The structural formula is:

Inactive Ingredients: Colloidal Silicon Dioxide, Anhydrous Lactose, Magnesium Stearate, Microcrystalline Cellulose, Sodium Starch Glycolate,

CLINICAL PHARMACOLOGY: The mechanism of the relief afforded by coichicine in acute attacks of gouty arthritis is not completely known, but studies on the processes involved

in precipitation of an acute attack have helped elucidate how this drug may exert its effects.

The drug is not an analgesic, does not relieve other types of pain or inflammation, and is of no value in other types of arthritis. It is not a diuratic and does not influence the renal excretion of uric acid or its level in the blood or the magnitude of the "miscible pool" of uric acid. It also does not after the sclubility of urate in the plasma.

Colchicine is not a uricosuric agent. An acute attack of gout apparently occurs as a result of an inflammatory reaction to crystals of monosodium urate that are deposited in the joint tissue from hyperuric body fluids; the reaction is aggravated as more urate crystals accumulate. The initial inflammatory response Involves local inflitration of granulocytes that phagocytize the urate crystals. Interference with these processes will pravent the development of an acute attack. Colohicine apparently exerts its effect by reducing the inflammatory response to the deposited crystals and also by diminishing phagocytosis. The deposition of uric acid is favored by an acid pH. In synovlat tissues and in leukocytes associated with inflammatory processes, lactic acid production is high, and this favors a local decrease in pH that anhances uric acid deposition. Colchicine diminishes lactic acid production by leukocytes directly and by diminishing phagocytosis and thereby interrupts the cycle of urate crystal deposition and inflammatory response that sestains the actic attack. The oxidation of glucose in phagocytizing as well as in non-phagocytizing leukocytes in vitro is suppressed by colchicine, this suppression may explain the diminished lactic acid production. The precise blochemical step that is effected by colchicine is not yet known.

That the antimitotic activity of colchicine is unrelated to its effectiveness in the treatment of acute gout is indicated by the fact that trimethylcolchicinic acid, an analog of colchicine, has no antimitotic activity except in extremely high doses.

INDICATIONS AND USAGE: Colchicine is indicated for the treatment of gout. It is effective in reliaving the pain of acute attacks, aspecially if therapy is begun early in the attack and in adequate dosage. Many therapists use colchicine as interval therapy to prevent acute attacks of goutt. It has no effect on nongouty arthritis or on uric acid metabolism.

CONTRAINDICATIONS: Colchicine is contraindicated in patients with gout who also have serious gastrointestinal, renal, or cardiac disorders.

WARNINGS: Colchicine can cause fetal harm when administered to a pregnant woman. If this drug is used during pregnancy, or if the patient becomes pregnant while taking it, the woman should be apprised of the potential hazard to the fetus. PRECAUTIONS: General Precautions: Colchicine should be administered with great caution to aged and debilitated patients, especially those with renal, gastrointestinal, or heart disease. Reduction in dosage is indicated if weakness, anorexia, nausea, vomiting, or diarrhea appears.

Drug Interactions: Colchicine has been shown to induce reversible malabsorption of vitamin B_{12} , apparently by alterlog the function of iteal mucosa. The possibility that colchicine may increase response to central nervous system depressants and to sympathomimetic agents if suggested by the results of experiments on animals.

Usage in Pregnancy: Pregnancy Category D'- See WARNINGS.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when colchicine is administered to a nursing woman.

Usage in Children: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: In full dosage, colchicine produces nausea, vomiting, or diarrhea. However, it is generally necessary to reach such dose levels for an adequate therapeutic effect. Paregoric may be given either concurrently or when diarrhea develops.

Prolonged administration may cause bone marrow depression, with agranulocytosis, thrombocytopeda, and aplastic anemia. Peripheral neuritis and depilation have also been reported.

OVERDOSAGE: There is usually a latent period between overdosage and the onset of symptoms, regardless of the route of administration. The lethal dose of colchiche has been estimated to be 65 mg. However, deaths have been reported with as little as 8 mg, although higher doses have been taken without fatal results.

The first symptoms to appear are gastrointestinal; nausea, vomiting, abdominal pain, and diarrhea. The diarrhea may be severe and bloody owing to hemorrhagic gastroenterior. To controi the diarrhea and cramps, paregoric is usually administered. Burning sensations in the throat, stomach, and skin may also occur. Extensive vascular damage may result in shock. The kidney may show avidence of damage by hematuria and oliquria, since it is an excretory site. Severe dehydration and hypotension develop. Muscular weakness is marked, and an ascending paralysis of the central nervous system may develop. The

EXHIBIT B

COLCHICINE TABLETS, USP

Rev. 06/08 Rx Only

DESCRIPTION: Colchicine is an alkaloid prepared from the dried corms and seeds of Colchicum autumnale, the autumn crocus or meadow saffron. It is a pale yellow powder soluble in water in a 1:25 dilution.

Colchicine Tablets, USP are an oral anti-Inflammatory agent. The chemical name for colchicine is (S)N-(5,6,7,9-tetrahydro-1,2,3, 10-tetra-methoxy-9-oxobenzo [alpha] heptalen-7-yl) acetamide.

Colchicine has the following structural formula:

Each tablet contains 0.6 mg (1/100 grain) colchicine USP and the following inactive ingredients: colloidal silicon dioxide, lactose anhydrous, magnesium stearate, microcrystalline cellulose, and sodium starch glycolate.

CLINICAL PHARMACOLOGY: The exact mechanism of action of colchicine in gout is not completely known, but it involves (1) a reduction in lactic acid production by leukocytes, which results in a decrease in uric acid deposition, and (2) a reduction in phagocytosis, with abatement of the inflammatory response.

Colchicine is not an analgesic, though it relieves pain in acute attacks of gout. It is not a uricosuric agent and will not prevent progression of gout to chronic gouty arthritis. It does have a prophylactic, suppressive effect that helps to reduce the incidence of acute attacks and to relieve the residual pain and mild discomfort that patients with gout occasionally feel.

In man and certain other animals, colchicine can produce a temporary leukopenia that is followed by leukocytosis. Colchicine has other pharmacologic actions in animals: It alters neuromuscular function, intensifies gastrointestinal activity by neurogenic stimulation, increases sensitivity to central depressants, heightens response to sympathomimetic compounds, depresses the respiratory center, constricts blood vessels, causes hypertension by central vasomotor stimulation, and lowers body temperature.

Cotchicine is rapidly absorbed after oral administration. Large amounts of the drug and metabolites enter the intestinal tract in bile and intestinal secretions. High concentrations of cotchicine are found in the kidney, liver, and spleen, as well. Cotchicine does not appear to be tightly bound to serum protein, hence the drug rapidly leaves the blood stream. Excretion occurs primarily by billiary and renal routes.

INDICATIONS AND USAGE: Colchicine is specifically indicated for treatment and relief of pain in attacks of acute gouty arthritis. It is also recommended for regular use between attacks as a prophylactic measure, and is often effective in aborting an attack when taken at the first sign of articular discomfort.

CONTRAINDICATIONS: Colchicine is contraindicated in patients with a known hypersensitivity to the drug, in those with serious gastrointestinal, renal, hepatic, or cardiac disorders, and in those with blood dyscrasias.

WARNINGS: Colchicine arrests cell division in animals and plants. It has adversely affected spermatogenesis in humans and in some animal species under certain conditions.

PRECAUTIONS: General: Colchicine should be administered with caution to aged or debilitated patients, and to those with early manifestations of gastrointestinal, renal, hepatic, cardiac or hematological disorders (See CONTRAINDICATIONS).

If nausea, vomiting or diarrhea occurs, the drug should be discontinued.

Laboratory Tests: In patients receiving long-term therapy, periodic blood counts should be done.

Drug Interactions: Colchicine is inhibited by acidifying agents.

The action of colchicine is potentiated by alkalinizing agents.

Colchicine may increase sensitivity to CNS depressants.

Response to sympathomimetic agents may be enhanced by colchicine.

Laboratory Test Interactions: Colchicine therapy may cause elevated alkaline phosphatase and SGOT values.

Decreased thrombocyte values may be obtained during colchicine therapy.

Colchicine may cause false positive results when testing urine for RBCs or hemoglobin.

Carcinogenesis: Data in the literature does not indicate colchicine as a carcinogenic agent.

Fertility: See WARNINGS section for information on impairment of fertility.

Pregnancy: Pregnancy Category C. Colchicine has been shown to be teratogenic in mice when given doses of 1.25 mg/kg and 1.5 mg/kg and in hamsters when given 10 mg/kg. There are no adequate and well-controlled studies in pregnant women. Colchicine should be used during pregnancy only if the potential benefit to the patient justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when colchiolne is administered to a nursing woman.



COLCHICINE TABLETS, USP Rev. 06/08 Rx Only ADVERSE REACTIONS: Adverse reactions in decreasing order of severity are: bone marrow depression with aplastic anemia, with agranulocytosis or with thrombocytopenia may occur in patients receiving long-term therapy. Peripherial neuritis, purpura, myopathy, loss of hair, and reversible azoospermia have also been reported.

Vomiting, diarrhea, and nausea may occur with colchicine therapy, especially when maximal doses are necessary for a therapeutic effect. To avoid more serious toxicity, the drug should be discontinued when these symptoms appear, regardless of whether or not joint pain has been relieved.

Dermatoses have been reported. Hypersentivity reactions may occur infrequently.

OVERDOSAGE: The onset of toxic effects is usually delayed for several hours or more after the ingestion of an acute overdose. Nausea, vomiting, abdominal pain, and diarrhea occur first.

The diarrhea may be bloody due to hemorrhagic gastroenteritis. Burning sensations of the throat, stomach, and skin may be prominent symptoms. Extensive vascular damage may result in shock. Kidney damage, evidenced by hematuria and oliguria, may occur. Muscular weakness may be marked, and ascending paralysis of the central nervous system may develop; the patient usually remains conscious. Delirium and convulsions may occur. Death may result due to respiratory arrest.

Although death from the ingestion of as little as 7 mg has been reported, much larger doses have been survived.

Treatment of colchicine poisoning should begin with gastric lavage and measures to prevent shock. Recent studies appear to support the use of hemodiallysis or pertinneal dialysis as part of the treatment of acute overdosage in addition to gastric lavage. Symptomatic and supportive treatment may include atropine and morphine for the relief of abdominal pain, and artificial respiration with oxygen to combat respiratory distress. No specific antidote is known.

DOSAGE AND ADMINISTRATION: Colchicine tablets are administered orally.

For Acute Gouty Arthritis – The usual dose to relieve or abort an attack is 0.6 mg (one tablet) to 1.2 mg (2 tablets). This dose may be followed by one tablet every hour or two tablets every two hours, until pain is relieved or until diarnhea ensues. Each patient should learn the dose he/she needs and keep the medication at hand for use at the first sign of an attack. After the initial dose, it is sometimes sufficient to take one tablet every two or three hours. The drug should be stopped if there is gastrointestinal discomfort or diarrhea. (Opiates may be needed to control diarnhea). In subsequent attacks, the patient should be able to judge his/her medication requirement accurately enough to stop short of his/her "diarrheal dose." The total amount of colchicine needed to control pain and inflammation during an attack usually ranges from 4 mg to 8 mg. Articular pain and swelling typically abate within 12 hours and are usually gone in 24 to 48 hours. An interval of three days between colchicine courses is advised in order to minimize the possibility of cumulative toxicity.

If corticotrophin (ACTH) is administered for treatment of an attack of acute gouty arthritis, it is recommended that colchicine also be given in doses of at least 1 mg per day, and that the latter be continued for a few days after the hormone is withdrawn.

For Prophylaxis During Intercritical Periods – To reduce the frequency of paroxysms and lessen their severity, colchicine may be administered continuously. In patients who have less than one attack per year, the usual dose is one tablet per day, three or four days a week. For cases involving more than one attack per year, the usual dose is one tablet every day; severe cases may require two or three tablets daily.

For Prophylaxis Against Attacks of Gout in Patients Undergoing Surgery — In patients with gout, attacks may be precipitated by even a minor surgical procedure. Colchicine, one 0.6 mg tablet three times a day, should be administered for three days before and three days after surgery.

HOW SUPPLIED: Colchicine Tablets, USP 0.6 mg (1/100 grain) are white, round, unscored, shallow concave compressed tablets imprinted "West-ward 201".

Bottles of 100 tablets Bottles of 1000 tablets Unit Dose Boxes of 100 tablets

Dispense in a tight, light-resistant container as defined in the USP using a child-resistant clo-

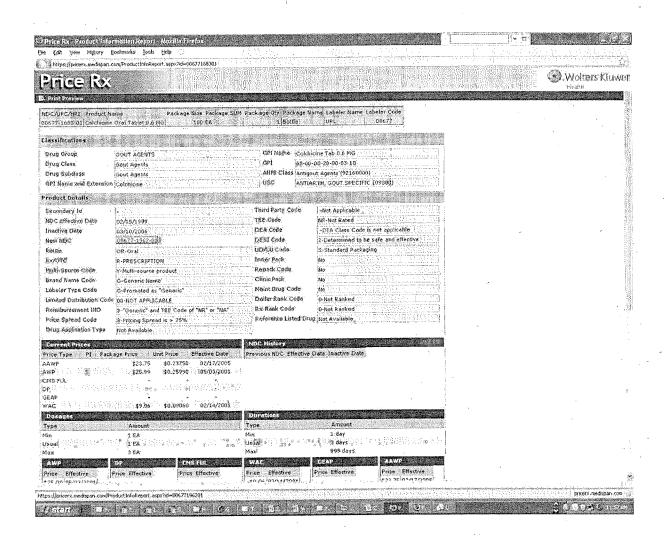
Store at 20-25°C - (68-77°F) [See USP Controlled Room Temperature]

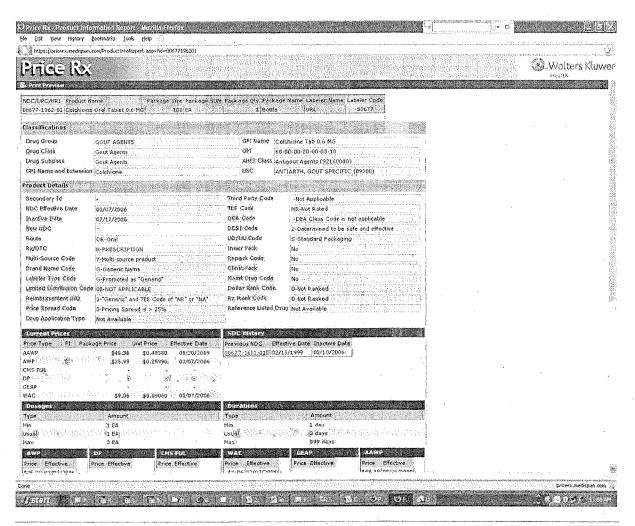
Protect from light and moisture.

Manufactured by: West-ward Pharmaceutical Corp Eatontown, NJ 07724

Rev 06/08

EXHIBIT C





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